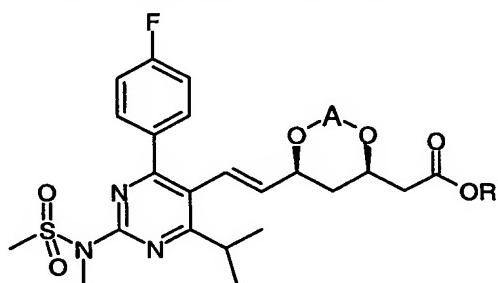


Claims

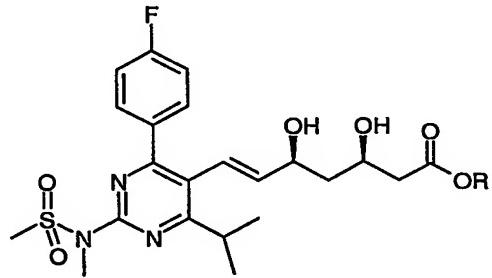
1. A process for the manufacture of the calcium salt of (*E*)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl](3*R*,5*S*)-3,5-dihydroxyhept-6-
5 enoic acid, comprising:

a) acid hydrolysis of an acetal protecting group in a compound of the formula (7)



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wherein A is an acetal or ketal protecting group and R is (1-6C)alkyl, and isolation of a resulting crystalline compound of the formula (8);

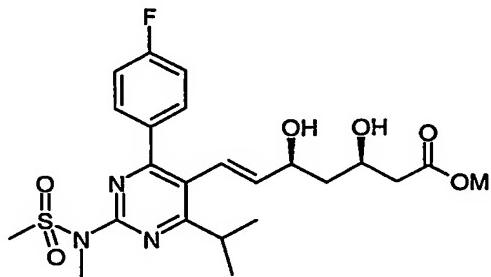


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b) optional recrystallisation of the compound of the formula (8);

c) hydrolysis of the ester group in the compound (8) to give a dihydroxy carboxylate derivative (9) (wherein M is hydrogen or a metal counterion other than calcium) or a compound of the formula (1); and

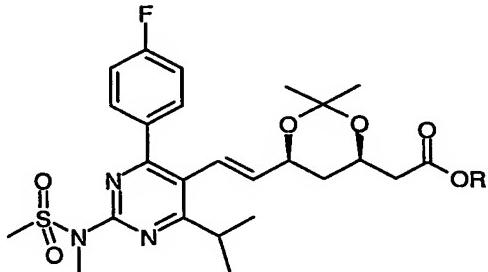


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d) where necessary, conversion of a compound of the formula (9) into a compound of the formula (1).

2. A process as claimed in Claim 1 wherein the compound of the formula (7) is a
5 compound of the formula (7a).



7a

3. A process for the manufacture of the calcium salt of (*E*)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl](3*R*,5*S*)-3,5-dihydroxyhept-6-
10 enoic acid, from a crystalline compound of formula (8) as claimed in steps c) and d) of Claim
1.

15 4. A process as claimed in Claim 1 or Claim 2 or Claim 3 wherein R is methyl, ethyl,
iso-propyl, tert-butyl or hexyl.

5. A process as claimed in any one of Claims 1 to 4 wherein R is ethyl, iso-propyl or tert-butyl.

20 6. A crystalline compound of the formula 7 as defined in Claim 1, which crystalline
compound is methyl (*E*)-(6-{2-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl]vinyl}(4*R*,6*S*)-2,2-dimethyl[1,3]dioxan-4-
yl)acetate having an X-ray powder diffraction pattern with peaks at 2-theta = 9.5, 13.6 and
17.5.

25 7. A crystalline compound of the formula 7 as defined in Claim 1, which crystalline
compound is ethyl (*E*)-(6-{2-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl]vinyl}(4*R*,6*S*)-2,2-dimethyl[1,3]dioxan-4-

yl)acetate having an X-ray powder diffraction pattern with peaks at 2-theta = 15.9, 18.4 and 19.5.

8. A crystalline compound of the formula 7 as defined in Claim 1, which crystalline compound is iso-propyl (E)-(6-{2-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl]vinyl}(4R,6S)-2,2-dimethyl[1,3]dioxan-4-yl)acetate having an X-ray powder diffraction pattern with peaks at 2-theta = 7.8, 11.6 and 15.5.

10 9. A crystalline compound of the formula 7 as defined in Claim 1, which crystalline compound is n-hexyl (E)-(6-{2-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl]vinyl}(4R,6S)-2,2-dimethyl[1,3]dioxan-4-yl)acetate having an X-ray powder diffraction pattern with peaks at 2-theta = 5.3, 7.1 and 18.9.

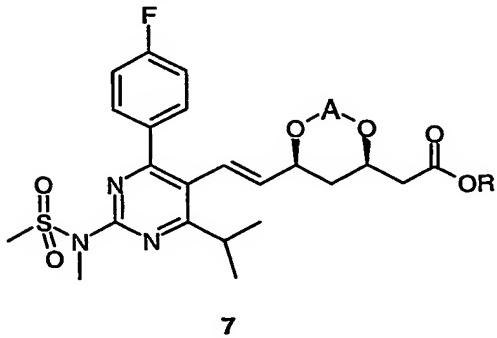
15 10. A crystalline compound of the formula 8 as defined in Claim 1, which crystalline compound is ethyl-(E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl](3R,5S)-3,5-dihydroxyhept-6-enoate having an X-ray powder diffraction pattern with peaks at 2-theta = 8.1, 11.3 and 19.9.

20 11. A crystalline compound of the formula 8 as defined in Claim 1, which crystalline compound is iso-propyl-(E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl](3R,5S)-3,5-dihydroxyhept-6-enoate having an X-ray powder diffraction pattern with peaks at 2-theta = 9.8, 17.3 and 21.1.

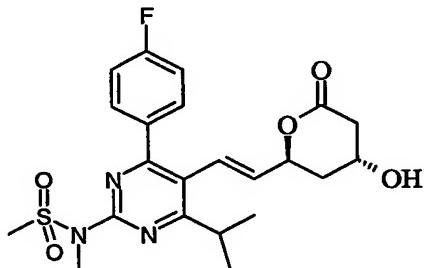
25 12. A crystalline compound of the formula 8 as defined in Claim 1, which crystalline compound is tert-butyl-(E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl](3R,5S)-3,5-dihydroxyhept-6-enoate having an X-ray powder diffraction pattern with peaks at 2-theta = 18.2, 19.9 and 20.8.

30 13. A process for the manufacture of the calcium salt of (E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl](3R,5S)-3,5-dihydroxyhept-6-enoic acid, comprising:

a) acid hydrolysis of an acetal protecting group in a compound of the formula (7)



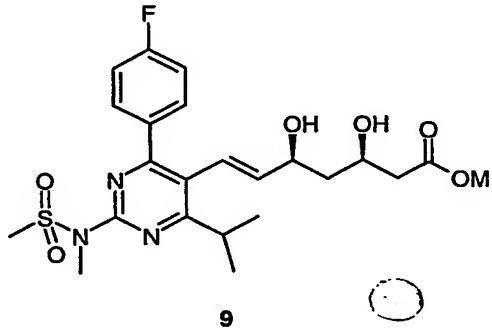
wherein A is an acetal or ketal protecting group and R is (1-6C)alkyl, and isolation of the resulting crystalline compound of the formula (10);



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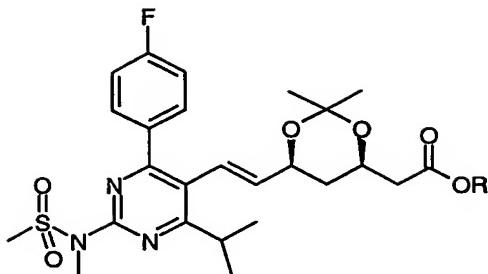
b) optional recrystallisation of the compound of the formula (10);

c) hydrolysis of the compound of formula (10) to give a dihydroxy carboxylate derivative (9) (wherein M is a metal counterion other than calcium) or a compound of the formula (1); and



10 d) where necessary, conversion of a compound of the formula (9) into a compound of the formula (1).

14. A process as claimed in Claim 13 wherein the compound of the formula (7) is a compound of the formula (7a).



7a

15. A process for the manufacture of the calcium salt of (*E*)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl](3*R*,5*S*)-3,5-dihydroxyhept-6-
5 enoic acid, from a crystalline compound of formula (10) as claimed in steps b) and c) of
Claim 13.

16. Crystalline (*E*)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl](3*R*,5*S*)-3,5-dihydroxyhept-6-enoic acid-(3,6)-
10 lactone having an X-ray powder diffraction pattern with peaks at 2-theta = 7.9, 11.9, 15.9,
20.3, 21.7 and 22.5.

17. A process for formation of amorphous bis[(*E*)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl](3*R*,5*S*)-3,5-dihydroxyhept-6-enoic acid]
15 calcium salt comprising isolation of a crystalline compound as claimed in Claim 16 from a solution and subsequent conversion to the amorphous form of bis[(*E*)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl](3*R*,5*S*)-3,5-dihydroxyhept-6-enoic acid] calcium salt.

20. 18. The use of a compound as claimed in Claim 16 as a processing aid for isolation of amorphous bis[(*E*)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl](3*R*,5*S*)-3,5-dihydroxyhept-6-enoic acid] calcium salt.

25. 19. The use of a compound as claimed in Claim 16 as a processing aid for recovery of amorphous bis[(*E*)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl](3*R*,5*S*)-3,5-dihydroxyhept-6-enoic acid] calcium salt from waste solutions.

20. The use of a compound as claimed in Claim 16 as an intermediate in the manufacture of amorphous bis[(E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl](3R,5S)-3,5-dihydroxyhept-6-enoic acid] calcium salt.